

**A CLINICOPATHOLOGICAL AND
IMMUNOFLUORESCENCE
STUDY OF LICHEN PLANUS**

*Dissertation Submitted in partial fulfillment
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CERTIFICATE

This is to certify that this dissertation titled “A clinicopathological and immunofluorescence study of lichen planus” submitted by **DR.G.LAKSHMI PRIYA** to the TamilNadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch- XII A, is a bonafide research work carried out by her under direct supervision and guidance.

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DECLARATION

I, **Dr.G. LAKSHMI PRIYA**, solemnly declare that the dissertation titled “A clinicopathological and immunofluorescence study of lichen planus” has been prepared by me. This is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai**, in partial fulfillment of the regulations for the award of MD degree branch – XII A Dermato venereo leprology.

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INTRODUCTION

Lichen planus is a papulosquamous disease of the skin and mucous membranes. It is derived from two words, 'leichen' in Greek meaning tree moss and 'planus' in Latin meaning flat. Lichen planus is worldwide in distribution with a variable incidence. It is considered to be due to cell mediated immune response to an epidermal antigen in genetically predisposed persons. Lichen planus has been found to be associated with certain infections and autoimmune diseases.

In its classic presentation, the disease is characterized by pruritic violaceous papules most commonly on the extremities of middle aged adults. It may be accompanied by oral and genital mucosal involvement. Hair and nails may also be affected. Besides the typical lesions, there are many variants of the disease.

The course of the disease is unpredictable. It generally persists for a period of several months to years. Sometimes it may follow a chronic relapsing course. The duration varies according to the extent and site of involvement and the morphology of the lesions.

Though this condition is mostly self-limiting, sometimes the patient may have considerable discomfort and disability. The lesions may heal with pigmentary changes and scarring. Malignant transformation may occur rarely.

Biopsy of fully developed lesions of lichen planus shows characteristic histological changes. Characteristic staining patterns are observed in the immunofluorescence study of the lesions.

Treatment options are based on the extent and severity of the disease. Symptomatic treatment is usually sufficient. In severe cutaneous and mucosal lichen planus, various other treatment approaches are useful. Glucocorticoids (topical, intralesional, systemic), cyclosporine, antimalarials, dapsone, thalidomide, azathioprine, phototherapy, doxycycline, interferons have been found to be effective.

REVIEW OF LITERATURE

HISTORICAL ASPECTS:

- Hebra first described the disease as leichen ruber.
- In 1869, Erasmus Wilson named the condition leichen planus.
- Kaposi described lichen ruber pemphigoides in 1892.
- In 1895, Louis Federic Wickham described whitish streaks on the surface of the papules.
- Histologic findings were elaborated by Darier in 1909.
- Scalp and follicular involvement reported initially by Graham Little in 1919.
- In 1935, Gougerot described the entity, invisible pigmented lichen planus.
- In 1956, Shima described lichen planus pigmentosus.
- In 1982, Pelisse et al described vulvovaginal gingival lichen planus.
- In 1993, Cribier et al described peno gingival lichen planus.
- In 1983, Olsen et al demonstrated lichen planus specific antigen by indirect immunofluorescence technique using autologous lesional skin¹.

EPIDEMIOLOGICAL ASPECTS OF LICHEN PLANUS

INCIDENCE:

The exact incidence and prevalence of LP are unknown, but the overall prevalence is believed to be less than 1% of the general population². Estimates

between 0.14 to 0.80% have been reported worldwide. An incidence of 0.38% has been reported from India³.

AGE:

LP most commonly affects middle aged adults though any age can be affected. Childhood LP is rare⁴. About 2/3rd cases occur between 30-60 years of age⁴. It is less common in very young and elderly.

SEX:

LP affects both sexes. A slight female preponderance has been reported². Males have an earlier age of onset (4th decade) than females (5th decade).

RACE:

No racial predilection has been noted⁵.

SEASONAL FACTORS:

No seasonal variation has been reported by some authors. One study reported a high incidence in December and January⁶.

FAMILIAL FORM:

A familial form of the disease exists but is rare⁷. Monozygotic twins may be affected. Association with HLA haplotypes HLA-B7,-Aw19,-B18,-Cw8 noted in familial forms.

ETIOPATHOGENESIS OF LP:

Exact cause of LP is not known. Immunological reaction plays role in the pathogenesis of LP. There is evidence of genetic and environmental influences.

HLA-B7,-Aw19,-B18,-Cw8 are associated with familial LP¹⁰. In nonfamilial cases, HLA-A3,-A5,-B8,-Bw35 are more common⁸. HLA-B8 is more common in patients with oral LP⁹.

Infectious agents, drugs, stress, allogenic cells are known to be involved in the pathogenesis of LP and lichenoid reactions. Hepatitis C virus infection has been associated with LP¹⁰.

Drugs like antimalarials, gold, frusemide, thiazides, penicillamine and spironolactone are known to cause LP like lesions¹¹. Dental amalgam materials are known to cause oral lichenoid reactions¹².

Studies have shown that LP represents a cell-mediated immune response to an induced antigenic change in the epidermal cells in a genetically predisposed individual¹³. CD8+ infiltrates in the lesional skin recognize a MHC Class I antigen called lichen planus specific antigen (LPSA), the exact nature of which is unknown. This may be an auto-reactive peptide or exogenous antigen such as altered protein, drug, contact allergen and viral or other infectious agent¹⁴.

The pathogenic role of HCV in the development of LP is still unclear. Nevertheless, demonstration of HCV RNA in epithelial cells of oral mucosa and skin lesions of patients with LP would lead to the theory that direct

action of the virus is involved. HCV could be a potential antigen presented by Langerhans cells, followed by activation and migration of lymphocytes resulting in damage to basal cells via cytokines of cytotoxic T cells. The virus may alter epithelial antigenicity at sites of mucocutaneous replication leading either to direct activation of cytotoxic T cells or to production of antibodies against epithelial antigens¹⁵.

Activation of cell mediated immune response destined towards keratinocyte apoptosis is the prime event in the pathogenesis of LP. The process involves three sequential stages:

1. LPSA recognition

2. cytotoxic lymphocyte activation

3. keratinocyte apoptosis

Antigen recognition is followed by CD8⁺ T cell activation. There is release of IL-2, IL-4, IFN γ , TNF α . IFN γ enhances expression of adhesion molecules ICAM-1, VCAM-1 by basal cells, Langerhans cells & other dendritic cells. There is increased concentration of collagen IV, collagen VII, laminin 5 which act as ligands for β 1 integrin on the surface of lymphocytes. The interaction between lymphocytes & basement membrane targets metalloproteinases and the process leads to basement membrane disruption¹⁶.

Mechanism of keratinocyte apoptosis:

- T cell secreted TNF α binds to TNF α R1 receptor on keratinocyte surface.
- T cell surface CD95 L (Fas ligand) binds to CD95 (Fas) on the keratinocytes.
- T cell secreted Granzyme B enters the keratinocyte via perforin induced membrane pores.

All these mechanisms activate caspase resulting in keratinocyte apoptosis¹⁷.

CLINICAL FEATURES:

The classical lesions of cutaneous LP are violaceous, flat topped polygonal papules associated with intense itching. The sites of predilection are flexor surface of wrists, trunk & thighs¹⁸. Oral cavity, genitals, nails and scalp may also

be involved¹⁹. Oral involvement may be the only manifestation²⁰. Involvement of face, palms, soles may also be present²¹.

Lesions appear along scratch marks or trauma. This is known as Koebner's (isomorphic) phenomenon. Fine, white reticulate pattern on the surface of the papules known as Wickham's striae is seen which is better visualized with a hand lens after applying oil. The lesions generally heal with hyperpigmentation.

Classification of lichen planus ²⁸:

Based on lesional morphology:

Hypertrophic LP

Atrophic LP

Guttate (eruptive) LP

Annular LP

Follicular LP

Linear LP

Vesiculobullous LP

Ulcerative LP

LP pigmentosus

Based on site of involvement:

Mucosal LP

Palmoplantar LP

Nail LP

Inverse LP

Special forms:

Drug induced LP

Actinic LP

LP pemphigoides

Lichen planus- lupus erythematosus overlap

HYPERTROPHIC LP:

Verrucous plaques occur,commonly over shins, ankles²².There is central depigmentation with surrounding hyperpigmented rim.The lesions are intensely pruritic and heal with scarring.They may persist for years.Squamous cell carcinoma may arise from long standing lesions²³.

ATROPHIC LP:

It is a rare form with well defined papuloplaque lesions with central atrophy. Usually typical papules are present at the margins²⁴.

ANNULAR LP:

This type is commonly seen on glans and shaft of penis. Central atrophy surrounded by a thin rim of active erythema is characteristic²⁵.The lesions tend to have a chronic course.

LINEAR LP:

This form represents only 0.25% of the different clinical patterns. It is more common in childhood. Sometimes, it may follow dermatomes (segmental or zosteriform) or lines of Blaschko²⁶.

GUTTATE OR ERUPTIVE LP:

Multiple, small erythematous lesions, pinhead to 1 cm size occur as recurrent crops in a widespread, generalized distribution²⁷.

FOLLICULAR LP:

It is also called as Lichen planopilaris. It presents as violaceous or pigmented follicular hyperkeratotic papules on trunk, medial aspect of extremities, scalp.

Cicatricial alopecia is a sequelae. In Graham Little Piccardi Lassueur syndrome, there is follicular LP of scalp or body, multifocal cicatricial alopecia of scalp and non cicatricial alopecia of axilla and pubic areas²⁹.

ULCERATIVE LP:

This presents as chronic, disabling, painful ulceration of the soles. It may cause permanent loss of toe nails. This type is important because it may be a site for malignant transformation³⁰.

LICHEN PLANUS PIGMENTOSUS:

This form is mainly seen in darker races. It is characterized by slate gray to dark brown macules over sunexposed areas, trunk and flexures. The lesions are asymptomatic and may be patchy, reticular, follicular or diffuse. Some believe it to be similar to ashy dermatosis³¹.

INVERSE LP:

Flexural sites like axillae, groin, inframammary region are predominantly affected.

ACTINIC LP:

It is also called as LP subtropicus & is seen in young adults in tropical countries. Sunlight is considered as predisposing factor³². Well defined

violaceous patches surrounded by a hypopigmented rim is seen mainly over the face, neck and dorsum of hands.

BULLOUS LP:

Vesiculobullous lesions may develop over the LP lesions during acute flare. Familial bullous LP is a rare autosomal dominant condition with bullous lesions on extremities. It has an earlier onset and widespread distribution³³.

LP PEMPHIGOIDES:

It is a rare variant with features of lichen planus and bullous pemphigoid. Tense bullae occur on extremities from both involved and uninvolved skin. Degeneration of basal cells leads to exposure of basement membrane antigens which stimulate the production of circulating antibodies to BP 180 KDa & BP 200 KDa antigens³⁴.

ORAL LP:

Upto 65% of patients with cutaneous LP have oral involvement. Isolated oral involvement can occur in about 15-35%³⁵. Sites of involvement are buccal mucosa, gingiva, tongue, palate & lips. The subtypes are reticulate, erosive or ulcerative, bullous, atrophic & plaque types. Reticulate pattern is the most common with irregular atrophic plaques with white streaks in a lacy pattern over the buccal mucosa. Oral LP may be asymptomatic or cause pain and

burning sensation. Oral LP especially the erosive type is prone for malignant transformation³⁶.

GENITAL LP:

This may occur alone or with oral or with generalized involvement. In females, painful vulval erosions with lacy reticulate borders occur. Scarring may occur. A variant of mucosal LP termed as vulvovaginal gingival syndrome is characterized by erosions and desquamation of vulva, vagina & gingiva³⁷. A male equivalent of this syndrome has been described as penogingival syndrome. In males, annular LP is more common. Lesions are seen over glans, shaft of penis, prepuce and scrotum³⁸.

NAIL LP:

Isolated nail LP is rare and it may cause twenty nail dystrophy³⁹. Nail is involved in 10-15% cases. The most common findings are nail plate thinning, longitudinal ridging, onychoschizia, onychorrhexis and sometimes anonychia⁴⁰. Pterygium is a classical finding.

PALMO PLANTAR LP:

It presents as yellowish hyperkeratotic plaques commonly over lateral margins of fingers and instep of sole⁴¹.

LUPUS ERYTHEMATOSUS/LICHEN PLANUS OVERLAP SYNDROME:

This shows clinical, histological and immunopathological characteristics of both disorders. It may occur as bluish red atrophic plaques or verrucous papules and nodules over photodistributed areas or acral portion of extremities⁴².

COMPLICATIONS

- Generalised LP lesions may give rise to erythroderma⁴³.
- Lichen planopilaris may lead to scarring alopecia⁴⁴.
- Nail LP may result in anonychia or dystrophy⁴⁵.
- post inflammatory pigmentary changes.
- Risk of malignant transformation in certain variants like oral LP, hypertrophic LP, ulcerative LP^{46,47}.

ASSOCIATED CONDITIONS

In the past few years, lichen planus has been linked to HCV infection, with studies demonstrating a higher prevalence of anti-HCV antibody titers in patients with cutaneous and oral lichen planus, compared with control subjects.

The reported rates of association have differed widely, probably because of varying study design, oral versus cutaneous lichen planus and geography⁴⁸⁻

⁵². Clinical variants associated mostly are oral LP, rarely eruptive and linear LP^{51,53,54}.

Cutaneous lesions which have been reported in association with LP are alopecia areata⁶²⁻⁶⁴, vitiligo⁶², morphea^{65,67}, lichen sclerosis⁶⁷, dermatomyositis⁶⁸, systemic lupus erythematosus⁶⁶, pemphigus vulgaris⁶⁹ and paraneoplastic pemphigus⁷⁰.

LP has been reported in association with diabetes mellitus particularly oral LP⁵⁵. The association of oral LP with diabetes & arterial hypertension is known as Grinspan syndrome.

The systemic disorders associated with lichen planus are ulcerative colitis⁵⁶, thymoma⁵⁷, myasthenia gravis⁵⁸, primary biliary cirrhosis⁵⁹, primary sclerosing cholangitis⁶⁰ and acquired hypogammaglobulinemia⁶¹.

DIAGNOSIS:

The diagnosis of lichen planus is clinical. In case of doubt, a biopsy should establish the diagnosis.

Histopathology of a classical lesion shows the following :

Compact orthokeratosis

Wedge shaped hypergranulosis (clinically Wickham's striae)

Vacuolar alteration of basal layer⁷¹

Band-like lymphocytic infiltrate in close approximation to the epidermis

This constellation of findings is sufficiently diagnostic that a histologic diagnosis can be made in more than 90%⁷².

Civatte bodies:

They are necrotic keratinocytes present in most cases in lower epidermis and especially in papillary dermis. They are also known as colloid, hyaline or cytoid bodies. They are 20 μ in diameter, homogeneous, eosinophilic PAS positive and diastase resistant⁷³.

Max Joseph space:

Occasionally, small areas of artifactual separation between epidermis and dermis are seen⁷⁴.

The rete ridges show irregular lengthening and some are pointed at their lower end, giving a saw toothed appearance⁷⁵.

The infiltrate in upper dermis is band like and sharply demarcated at its lower border and is composed almost entirely of lymphocytes intermingled with macrophages⁷⁶. A few eosinophils and plasma cells may be seen. Melanophages are seen in upper dermis due to damage of the basal layer and pigment incontinence⁷⁷.

Hypertrophic LP:

Considerable acanthosis, papillomatosis, hyperkeratosis and hypergranulosis are seen. The interface changes are discrete and often limited to the base of the rete ridges⁷⁸.

Atrophic LP:

There is thinning of the epidermis upto the granular layer and effacement of rete ridges⁷⁹.

Ulcerative LP:

Epidermal ulceration is present with typical changes of LP at the margin of the ulcer⁸⁰.

Follicular LP:

Orthokeratosis, follicular plugging and wedge shaped hypergranulosis of the infundibulum, vacuolar changes of basal layer of outer root sheath and necrotic keratinocytes are seen with focally dense band-like perifollicular lymphocytic infiltrate at the level of infundibulum and isthmus . Interfollicular epidermis is often spared. In later stages, perifollicular fibrosis& epidermal atrophy give rise to hour glass configuration⁸¹.

Bullous LP:

Typical features of LP with subepidermal bulla and heavy dermal infiltrate with numerous colloid bodies are seen⁸².

LP pemphigoides:

Biopsy of uninvolved skin shows subepidermal bulla with an infiltrate that is not band-like and which contains plenty of eosinophils⁸³.

Actinic LP:

There is thinning of epidermis towards the centre of the lesion with more evident pigmentary incontinence in upper dermis⁸⁴.

LP pigmentosus:

Typical features of LP seen with pronounced pigment incontinence extending to reticular dermis and less prominent inflammatory infiltrate⁸⁵.

LE/LP overlap:

A lichenoid reaction typical for LP and histological features of LE are usually present in the same biopsy⁸⁶.

Drug induced LP:

Parakeratosis, numerous eosinophils and perivascular inflammation are seen which are absent in classical LP.

Mucosal LP:

Epithelium is often atrophic. There is parakeratosis and absence of granular layer. There are fewer colloid bodies⁸⁷.

Nail LP:

Usual changes of LP are present. The granular layer which is normally absent, is present. Colloid bodies are rare⁸⁸.

DIRECT IMMUNOFLOUORESCENCE IN LICHEN PLANUS:

Procedure:

A 4 mm punch biopsy is taken from lesional skin.

If there is delay of more than 24 hours before processing, the specimen is kept in Michel's medium which contains 5% ammonium sulfate, magnesium sulfate, N-ethyl maleimide in citrate buffer (pH 7.25).

While processing, the specimen is washed several times in phosphate buffer saline and 5 micron thick sections are made. The sections are stained with IgG, IgA, IgM, fibrinogen and C3 antibodies labelled with fluorescein isothiocyanate and then visualized in fluorescent microscope⁸⁹.

DIF Pattern:

In LP, shaggy deposits of fibrinogen at the dermo epidermal junction is characteristic⁹⁰.

Necrotic keratinocytes are demonstrable in 87% of cases. They stain mainly for IgM but also for IgG, IgA, C3 and fibrin⁹¹.

In lichen planopilaris, deposition of IgM, IgA, IgG, C3 occurs at the level of infundibulum and isthmus. There is often deposition of fibrinogen in a shaggy pattern surrounding the affected follicles⁹².

In LP pemphigoides, DIF of perilesional skin shows IgG & C3 in linear pattern along BMZ⁹³.

In LE/LP overlap, the most common finding is presence of cytooid bodies staining with IgG, IgM & C3 intraepidermally or at BMZ. Linear to granular

deposition of IgM&C3 are observed occasionally. Shaggy deposition of fibrinogen at the BMZ is sometimes found⁹⁴.

INDIRECT IMMUNOFLUORESCENCE IN LICHEN PLANUS:

IIF is of particular help to differentiate atypical cases of LP from other dermatoses.

Lichen planus specific antigen (LPSA) can be demonstrated using the patient's serum & autologous lesional skin.

PROCEDURE:

A 4 mm punch biopsy is taken from lesional skin, snap frozen and sections are taken using cryostat.

5 ml of patient's blood is collected and serum is separated.

Serum (1:10 and 1:80 dilution) is incubated with lesional skin sections for one hour & washed in PBS.

It is then incubated with various fluorescein isothiocyanate conjugates for one hour & washed again in PBS. It is mounted in buffered glycerol and examined under fluorescent microscope⁹⁵.

IIF Pattern:

LPSA is specific for lichen planus and is found in 80% of patients. IIF using autologous lesional skin shows characteristic fluorescent IgG deposits in the upper epidermis at the level of stratum granulosum and stratum spinosum⁹⁶.

AIM OF THE STUDY

- 1.To find out the clinical profile of lichen planus seen among patients attending the skin OPD.
- 2.To find out the dermatological and systemic associations and complications if any.
- 3.To correlate the clinical and histopathological features of various types of LP.
- 4.To know the immunofluorescence patterns of LP.

Materials and Methods

The material for this study was from the patients attending the skin OPD, Government Rajaji Hospital, Madurai Medical College, Madurai during the period from July 2008 to July 2009.

Inclusion criteria:

Patients diagnosed clinically as lichen planus during the study period.

Exclusion criteria:

Patients who did not give consent for biopsy were not subjected to biopsy procedure but were included in the study of the clinical profile.

A total of 90 patients were clinically diagnosed as lichen planus during this period and were taken for the study. A detailed clinical history including duration, site of onset, symptoms, drug history, family history were elicited. A complete general examination, systemic examination and dermatological examination were made. Digital photographs were taken.

The morphology and distribution of skin lesions, presence of any other associated diseases were noted. Concomitant affection of mucosa, hair, nails, palms, soles, genital involvement was meticulously recorded.

Laboratory investigations like urine examination, blood sugar, urea, creatinine, liver function tests, anti HCV antibody, blood VDRL and complete hemogram were done.

Skin biopsy was done in 50 patients who gave informed consent. After thorough cleaning of the part to be biopsied with spirit, 2% lignocaine was infiltrated into the area and a bit of the lesional skin was removed by punch biopsy. The specimen were preserved in 10% formalin and submitted for histopathological examination to the department of Pathology, Madurai Medical College.

Out of the 50 patients in whom histopathological examination was done, direct immunofluorescence study could be done in only 20 patients due to financial constraints. The lesional skin was biopsied and specimen preserved in Michel's medium and sent to the department of Skin and STD, Kasturba hospital, Manipal.

OBSERVATIONS AND RESULTS

In this study, 90 cases of lichen planus were studied from the outpatient department of dermatology, Government Rajaji hospital, Madurai medical college, from July 2008 to July 2009. The following observations were made. Apart from the classical presentation which was seen in most patients, the other types of LP encountered were hypertrophic, eruptive, linear, annular, follicular, actinic, LP pigmentosus, LE/LP overlap and isolated oral LP.

Table 1: Clinical types of LP

Clinical type of LP	No of pts	Percentage(%)
Classical	60	66.66
Hypertrophic	10	11.11
Eruptive	4	4.44
LP pigmentosus	3	3.33
Linear	5	5.55
Isolated oral	2	2.22
Annular	2	2.22
Follicular	2	2.22
LE/LP overlap	1	1.11
Actinic	1	1.11

Classical lichen planus was the commonest type (67%), followed by hypertrophic type (11%), linear variant (5.5%), eruptive type (4%), lichen planus pigmentosus(3%). Isolated oral LP was seen in 2%. Annular LP, follicular LP, LE/LP overlap and actinic LP were the other types seen.

AGE DISTRIBUTION

Table 2. The age of onset:

Age of onset	Class	Er	LP Pigm	Oral	Ann	HT	Linear	Actinic	Foll	LE/LP
0-10	3	1	-	-	-	-	2	-	-	-
11-20	3	2	1	-	-	-	1	1	-	-
21-30	12	-	-	-	1	2	1	-	-	-
31-40	15	1	2	1	1	3	-	-	1	-
41-50	18	-	-	1	-	3	-	-	-	-
51-60	6	-	-	-	-	2	1	-	-	1
61-70	3	-	-	-	-	-	-	-	1	-

Total	60	4	3	2	2	10	5	1	2	-
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Class = classical

HT = hypertrophic

Er = eruptive

Foll = follicular

LP Pigm = LP pigmentosus

Ann = annular

Age group	Number	Percentage
0-10 yrs	6	6.67
11-20 yrs	8	8.88
21-30 yrs	16	17.77
31-40 yrs	24	26.66
41-50 yrs	22	24.44
51-60 yrs	10	11.11
61-70 yrs	4	4.44

The majority of patients were in the age group of 31-50 years .The number of patients in each age group were as follows:

Table 3:

Sex distribution:

44 patients were males and 46 were females.

Table 4: sex distribution

Types Of LP	Male	Female
Classical LP	27	33
Eruptive LP	3	1
LP Pigmentosus	1	2
Oral LP	-	2
Annular LP	2	-
Hypertrophic	7	3
Linear LP	3	2
Actinic LP	-	1
Follicular LP	1	1
LE/LP Overlap	-	1

Initial site of onset was limbs in 63%, trunk in 21%, face in 8%, genitals in 2% and oral mucosa in 6%. Papules were present in 79% and plaques were present in 14% of the cases. Koebner's phenomenon was seen in 33% of the patients.

Table 5: childhood LP:

S.no	Age	Sex	Clinical type	Mucosal Inv.	Palm/sole Inv.	Nail Inv.
1.	10 yrs	F	Classical	-	-	-
2.	11 yrs	M	Linear	-	-	-
3.	5 yrs	M	Classical	-	-	-
4.	6 yrs	F	Classical	-	-	P
5.	12 yrs	M	Eruptive	-	-	-
6.	4 yrs	M	Eruptive	-	-	-
7.	8 yrs	M	Linear	-	-	-
8.	8 yrs	F	Linear	-	-	-

Symptoms :

The presenting symptoms of the patients were itching in 73% and 7% had pain in the lesions involving oral mucosa and 20% were asymptomatic.

Mucosal involvement :

Oral mucosal involvement was seen in 19 patients and genital mucosal involvement was noted in 2 patients .

Table 6: Mucosal involvement :

Clinical type	Oral mucosa	Genital mucosa
Classical LP	13	-
Eruptive LP	-	-
LP Pigmentosus	-	-
Isolated oral LP	2	-
Annular LP	-	2
Hypertrophic LP	3	-
Linear LP	-	-
Actinic LP	-	-
Follicular LP	-	-
LE/LP Overlap	1	-

Oral mucosal involvement :

Patterns of oral mucosal involvement seen were reticular, erosive and plaque types.

Cheek mucosa and lips were the common sites affected.

Table 7: Patterns of oral mucosal involvement

Pattern	Reticular	Erosive	Plaque
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No of pts.	11	3	5
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Genital involvement :

Genital involvement was seen as annular lesions over glans penis in 2 patients and papules over shaft of penis and scrotum in 7 patients. Genital involvement was not present in the female patients.

Table 8: Genital involvement:

Types Of LP	No. Of Patients With genital Involvement
Classical LP	6
Eruptive LP	1

Annular LP

2

Nail involvement:

Nail involvement was seen in 16 cases. Longitudinal ridging, pterygium, thinning of nail plate, onychomadesis, trachyonychia were commonly seen.

Nail Involvement was present in 14 cases of classical LP and 2 cases of hypertrophic LP.

Table 9: Nail involvement:

Findings

No of pts.

Longitudinal ridging	4
Pterygium unguis	3
Nail plate thinning	2
Trachyonychia	2
Onychomadesis	2
Longitudinal melanonychia	1
onychoschizia	
Punctuate leuconychia	1
	1

Palmoplantar LP:

Palmoplantar involvement was seen in 18cases. It was seen in 14 cases of classical type, 3 cases of hypertrophic type and 1 case of eruptive LP.

Involvement of palms and soles was characterized by hyperkeratotic scaly plaques.

Table 10: Palmoplantar LP

Types Of LP	No. of pts with Palmo-plantar Involvement
Classical LP	14
Eruptive LP	1
LP Pigmentosus	-
Oral LP	-
Annular LP	-
Hypertrophic LP	3
Linear LP	-
Actinic LP	-
Follicular LP	-
LE/LP Overlap	-

Associated diseases:

The diseases which were found to be associated were diabetes mellitus, hypertension , vitiligo, albinism , alopecia areata and hypothyroidism.

Table 11: associated diseases:

Type of LP	DM	HT	Vo	AA	Albinism	hypothyroid
Classical LP	3	1	-	1	1	2
Hypertrophic	2	1	-	-	-	-
Oral LP	1	-	-	-	-	-
Actinic LP	-	-	1	-	-	-

The **direct immunofluorescence findings** were as follows:

Table 12:DIF findings:

Findings	Classical LP	Hypertrophic LP	LE/LP	LP Pigmentosus
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Coll oid Bod ies	IgG	2	1	-	-
	C3	3	2	-	2
	IgM	6	3	1	2
	IgA	4	2	-	1
	Fibrin	3	2	-	1
BM Z Dep osit s	Ragged Fibrin	13	4	1	2
	IgG	3	-	1	-
	C3	3	-	1	-

Biopsy Findings

- Classical LP
- HT LP
- Oral LP
- LP Pigmentosus
- Linear LP
- Follicular LP
- Actinic LP
- LE/LP
- Eruptive LP

Orthohyperkeratosis

- 26
- 9
-
-
- 2
- 2
-
- 1
- 2

Parakeratosis

- 2
-
- 2
-
-

	-
	-
	-
	-
Focal Hypergranulosis	26
	9
	-
	1
	2
	-
	-
	1
	2
Acanthosis	25
	9
	-
	1
	2
	-
	-
	-
	2
Epidermal thinning	
	-
	-
	-

	-
	-
	-
	1
	-
	-
Sawtooth rete	24
	9
	1
	1
	2
	-
	-
	-
	2
Follicular plugging	-
	-
	-
	-
	-
	2
	-
	1
	-
Basal layer degeneration	28

9
2
3
2
2
1
1
2

Pigment incontinence

27
9
2
3
2
2
1
1
2

Colloid bodies

10
4
-
3
-
-
1
1
-

Infiltrate
Band like lym.at BMZ

28
-
2
3
2
2
1
-
2

Lym. mainly at base of rete

-
9
-
-
-
-
-
-
-

perifollicular lym.

2

-

-

-

-

2

-

1

-

Eosinophil infiltrate

2

-

-

-

-

-

-

-

-

patchy lym.& perivascular inf.

-
-
-
-
-
-
-
- 1
-

Features of squamous cell carcinoma

-
- 1
-
-
-
-
-
-
-

DISCUSSION

Incidence:

In our study, the incidence of lichen planus was 0.16 percent among 57,684 new patients attending the Skin OPD during the period from July 2007-July 2008.

Age distribution:

The age of the patients ranged from 4 to 68 years. The majority of patients (46 patients or 51%) fall in the age group from 31-50 years which is similar to studies done by Singh et al and Bhattacharya et al^{97,98}. Various studies show that childhood involvement is uncommon¹⁰⁰⁻¹⁰². In our study, childhood LP was noted in 9%(8 patients).

Sex distribution:

Predominance of males was reported in few studies⁹⁷ while the reverse has also been reported⁹⁹. Equal ratio has also been reported⁹⁸. In our study, almost equal involvement was noted. 44 patients were males and 46 were females. In childhood LP, 5 were males and 3 were females with a male: female ratio of 1.6:1.

Clinical features:

Limbs are the most prevalent site of onset of LP as stated by Altman and Perry who reported a frequency of 89 percent¹⁰³. This was the case in our study, with initial limb affection of 57 patients (63%). The initial site of onset was trunk in 19 cases(21%), face in 7 cases(8%), genitals in 2% and oral mucosa

in 5 cases(6%). Papules were present in 79% and plaques were present in 14% of the cases.

Prior history of drug intake was present in 12 patients. Itching was the main complaint in 73% percent of our patients, which was severe in patients with hypertrophic lesions. Itching was relieved by rubbing in 60 percent and by scratching in 13 percent of patients. Scratching was sometimes evidenced by excoriations and scratch marks. Koebner's phenomenon was seen in 33% of the patients.

Classical lichen planus was the commonest type (67%) which is in concordance with the literature^{97-100,104}. Classical type was followed by hypertrophic type (11%), linear variant (5.5%), eruptive type (4%), lichen planus pigmentosus (3%). Isolated oral LP accounted for 2%. Annular LP was present in 2% and follicular LP was present in 2%. 1 case had features of LE/LP overlap and actinic LP was seen in one case. Classical, linear and eruptive types were seen in children.

Studies reveal predominance of the classic type among LP patients followed by the hypertrophic and the actinic varieties ^{97,98,105}. Our study shows predominance of classic LP followed by hypertrophic LP. However, linear variant which is reported to be relatively rare was the next common in our study. As a result of cutaneous mosaicism, individuals may have distinct cell populations within their skin that are more likely to develop a skin condition .

Linear LP is an example of this phenomenon and accounts for less than 0.2 percent of all patients with LP¹⁰⁶.

In one patient, zosteriform pattern on the trunk coexisting with linear pattern on the limb was seen. The patient had no past history of herpes zoster at the site of the lesion. Zosteriform configuration is reported to be rare¹⁰⁷⁻¹¹². Altman and Perry reported only 1 case out of 307 cases of LP.

Oral lesions:

Oral LP associated with cutaneous lesions was detected in 17 patients and 2 patients had isolated oral LP. Plaque type, erosive and reticular patterns were seen in 5,3,11 patients respectively. Cheek mucosa, lips, tongue, gingiva were affected. From the different types of oral lesions, the reticular type was the most prevalent and the buccal mucosa was the most common site affected, an observation supported by the literature¹¹⁹.

Genital lesions were observed in 9 male patients (10%). Genital LP appeared as annular plaques on glans penis in 2 patients and small papular lesions on shaft of penis, scrotum in 7 cases. Genital lesion was not present in any of the females.

Nail changes were seen in 16 patients (18%). Pterygium was detected only in 3 of the patients. Apart from pterygium formation, the changes which were noted were longitudinal ridging of the nails, onychomadesis, trachyonychia,

nail plate thinning, longitudinal melanonychia, onychoschizia & punctuate leuconychia.

Palmoplantar LP with accompanying skin involvement accounted for 20% of our cases. It was characterized by the presence of very pruriginous hyperkeratotic scaly plaques as reported in the literature .

Mucosal and palmoplantar involvement were not seen in the childhood cases. Only one case had nail involvement. This observation is similar to other studies¹²⁰.

HCV association:

Various studies conducted in different parts of the world have either proved or disproved a causative role for HCV in LP¹²¹⁻¹²⁵. It has been suggested that routine liver function tests and further screening on the basis of abnormal values will be a fair enough protocol to follow, especially in areas where the prevalence of HCV infection is low ¹²⁶.In our study ,abnormal LFT was seen in 5 patients. They were tested for anti HCV antibody and were found to be negative.

Other associations:

Diabetes mellitus was present in 6 patients(6.6%).Hypertension was present in 2 cases(2.2%).2 patients had hypothyroidism. Vitiligo was present in a case of actinic LP. Alopecia areata was seen in one patient. Lichen planus was seen in

an albino child as scaly nonpigmented itchy papules. Squamous cell carcinoma complicating a case of hypertrophic LP was seen.

Diabetes, hypertension , hypothyroidism are reported to be associated with lichen planus^{127,128}.

Ahmed et al reported a case of co-existence of vitiligo and actinic lichen planus with possibility of common aetiological background¹²⁹. Co-existence of two disorders may be due to a prominent immunological component in their pathogenesis. In vitiligo autoimmune hypothesis is suggested by its clinical association with number of disorders. In lichen planus, probably autoimmunity plays a role as suggested by Shuttleworth et al¹³⁰.

Histopathology :

The classical histopathological changes were seen in all the cases of lichen planus.

Epidermal changes were characterized by orthohyperkeratosis (84%), focal hypergranulosis (80%), and acanthosis (78%) with toothching of rete ridges (78%) and basal cell liquefaction (100%). Epidermal thinning was

observed in the case of lichen planus actinicus. Hypertrophic LP had more marked hyperkeratosis and acanthosis and follicular plugging was present in lichen planopilaris.

Dermal changes were characterized by a band-like inflammatory infiltrate predominantly of lymphocytes with a few macrophages hugging the dermo-epidermal junction in most of the cases. In lichen planopilaris, perifollicular involvement was present. A prominent perivascular infiltrate was observed in the case of LE/LP overlap.

Two cases of classical LP showed parakeratosis and prominent eosinophilic infiltrate in addition to the lymphocytic infiltrate. Both of them had history of drug intake, one patient was on captopril and the other patient was on chlorpromazine. A diagnosis of drug induced lichen planus was made based on the drug history and histological findings.

Both linear LP and eruptive LP showed features similar to classical type histologically.

Pigment incontinence in the form of melanophages was seen in the superficial dermis in all cases except one in the case of lichen planus in a child with albinism. Civatte bodies were seen in only 36% of cases. They were seen as round, eosinophilic bodies in the lower epidermis and papillary dermis. Colloid bodies were observed in large numbers in the case of actinic LP & LP

pigmentosus. Features of squamous cell carcinoma was seen in the biopsy of warty growth in a case of hypertrophic LP.

Direct immunofluorescence:

A ragged fibrin band at the basement membrane zone was the most characteristic finding, being seen in all the 20 patients. Colloid bodies demonstrating IgM, C3, IgG, or IgA were seen in 12 out of the 20 cases. Colloid bodies have been noted in other dermatoses but their occurrence in large numbers in the lower epidermis and upper dermis is characteristic of LP. In our study, CB's were noted in 60% of cases. Linear IgG, C3 at the BMZ with shaggy fibrinogen was seen in the case of LE/LP overlap. IgG, C3 deposition at the BMZ which resembled those of LE was present in three cases of classical LP. Kulthanan et al in their study noted shaggy fibrin deposition at the DEJ in 56% of cases & CB's in 22% of cases. Some of their patients also showed DIF features resembling LE¹³¹. In their study, Lim et al reported shaggy fibrin along BMZ in 93% of the cases, & colloid bodies in 87% of the cases. However they did not find any immunoglobulin deposition along the basement membrane¹³².

The simultaneous deposition of complement fragments, immunoglobulins and fibrin in lesions of LP point to the activation of complement and a fibrinogen cascade. These products in turn act as chemoattractants for leucocytes leading to the in

flammatory response in LP, which perpetuates the basal cell damage. Whether these events are a cause or effect of pathological processes in lichen planus needs to be elucidated.

Interesting observations:

Zosteriform LP:

A 60 year old male had **zosteriform LP** on trunk **coexisting with linear LP** in limb.

Dermatomal lichen planus can erupt following healed herpes zoster of the same location, an example of the Wolf isotopic response or in extremely rare cases, linear or segmental distributions appear de novo on previously normal, non-traumatized skin, as in our patient¹¹⁴⁻¹¹⁸. Although case reports of de novo dermatomal LP have been reported some authors believe that true zosteriform LP does not exist except in cases arising on the site of healed herpes zoster. However, Lutz presented two cases of zosteriform lichen planus without evidence of preceding viral disease¹¹³.

In our patient, the distribution of lesions followed the T9 dermatome. The patient denied prior history of herpes zoster. The eruption on the trunk seemed to follow a true dermatome rather than in the pattern the lines of Blaschko. In many of these cases, it is difficult to differentiate the two. So it remains unknown if there are two separate forms of unilateral, de novo lichen planus, one type arising in the lines of Blaschko (Blaschkonian lichen planus) and the other arising within one or more dermatomes. In our case, zosteriform pattern on the trunk was present in addition to linear pattern on the limb which is so far not reported in the literature.

LP in albino child:

Lichen planus presented as pruritic scaly reddish brown papules on trunk & limbs in a 4 year old child with albinism. Histology showed all the findings of a classical lichen planus except for pigment incontinence.

LE/LP overlap:

A 55 year old female presented with bluish red scaly papules and plaques on the lower lip, upper chest, legs and forearms.

Evaluation of laboratory data including antinuclear antibody were within normal limits.

Histopathologic examination revealed hyperkeratosis, hypergranulosis, follicular plugging, dermal mucin and perivascular & perifollicular infiltrate of lymphocytes with patchy lymphocytic infiltrate at BMZ. Vacuolar alteration of basal layer and colloid bodies were seen. DIF showed linear IgG, C3 at the BMZ with shaggy fibrinogen.

Our patient had the characteristic clinical and histological features of both LE and LP. Coexistence of these two diseases has been described by Romero et al¹³³. Jamison et al suggest such cases should be followed up to confirm whether these are coexistent diseases or unusual variant of LE¹³⁴.

Malignant change in hypertrophic LP:

Squamous cell carcinoma developing from lesion of hypertrophic LP was noted in one case. A 51 year old female presented with lesions over legs for 8 years. Over the last six months, a small, hard growth had appeared in left leg that enlarged to the present size. There was no history of trauma or any application of irritants at the site. A large verrucous growth with some ulceration and crusting over the surface was present. Regional lymph nodes were not palpable and systemic examination was normal. Biopsy specimens were obtained from

the edge and from the overlying tumor. The first one showed findings typical of hypertrophic LP. The second specimen showed features of a well-differentiated squamous cell carcinoma comprising of epidermal proliferation with horn pearls and scattered atypical mitotic figures. Neoplastic transformation of lichen planus is a rare event. However, squamous cell carcinoma may develop in 0.3%-3% of patients with the oral form of the disease¹³⁵. On the other hand, only about 30 cases arising in cutaneous lichen planus have been reported¹³⁶.

Summary

Incidence:

Lichen planus constituted 0.16 percent of the total patients diagnosed during the period of study.

Age:

51% of patients were between 31-50 years of age. Childhood LP accounted for about 9% of cases.

Sex:

No sexual predilection was seen.

Familial involvement& seasonal variation:

There was no family history and seasonal variation was not seen.

Morphology and distribution of lesions:

Papules were present in 79% and plaques were present in 14% of the cases. Initial site of onset was limbs in 63%, trunk in 21%, face in 8%, oral mucosa in 6% and genital mucosa in 2%. Oral mucosa was involved in 21%. Nail involvement was noted in 17%. Palmoplantar involvement was present in 20%. Koebner's phenomenon was seen in 33%.

Clinical patterns:

Classical LP was the commonest seen in 60 cases followed by hypertrophic LP seen in 10 cases. A linear pattern was seen in 5 cases. A zosteriform pattern in

trunk was present in one case of linear LP of the limb. 3 cases had LP pigmentosus ,4 patients had eruptive LP,1 had actinic LP and 2 patients had follicular LP. 1 patient had features of LE/LP overlap.Isolated oral LP and annular LP were present in 2 cases each.

Histopathology:

Histopathological features were consistent with classical LP in 30 cases , hypertrophic LP in 9 cases, Follicular LP in 2 , LP pigmentosus in 3, actinic LP in 1,oral LP in 2, LE/LP overlap in 1,drug induced LP in 2. Features of squamous cell carcinoma was present in the warty growth from a case of hypertrophic LP .

Immunofluorescence:

DIF study done in 20 patients showed ragged fibrinogen deposits in basement membrane zone in all the patients. Colloid bodies were seen in 60%. Linear IgG, C3 at the BMZ with shaggy fibrinogen was seen in the LE/LP overlap syndrome. Linear IgG,C3 at the BMZ with shaggy fibrinogen was also present in three cases of classical LP.

Associations:

In this study, the diseases which were found to be associated were diabetes mellitus, hypertension, hypothyroidism, vitiligo & alopecia areata .Interesting presentation of lichen planus in a case of albinism was seen.

Malignant change:

A case of hypertrophic LP developed squamous cell carcinoma.

Conclusion

1. The incidence of Lichen planus in this study was 0.16% .
2. Most of the patients were in 4th and 5th decade.
3. Classical type was the commonest followed by hypertrophic type & linear variant next in frequency.
4. Limbs were the most frequent initial site of onset.
5. Concomitant mucosal, genital, nail and palmoplantar involvement was common.
6. There was a complete correlation between clinical types and histopathological features in all the 50 patients biopsied.
7. The characteristic findings of ragged fibrin at BMZ and colloid bodies with IgM and C₃ & to a lesser extent with other classes of immunoglobulins were observed in the immunofluorescence study.
8. A case of zosteriform lichen planus coexisting with linear LP was present.
9. Association of other immune mediated diseases was noted.
10. Malignant change was observed in a case of hypertrophic lichen planus.
11. Interesting presentation of lichen planus in a case of albinism was noted.

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PROFORMA

Name:

Occupation:

Age:

Income:

Sex:

Socioeconomic Status:

Address:

H/o Skin lesion:

- Duration
- Site of first lesion
- Evolution of the lesion

H/o Mucosal involvement:

- Oral
- Genital

H/o pruritus / burning / pain over the lesions

Healing spontaneously or with treatment

Heals with hyperpigmentation or hypopigmentation

H/o drug intake / infection

H/o lesions following trauma

General H/o:

- HT / TB / DM / Heart disease
- Malignancy
- Smoking / alcohol
- Marital status
- Family H/o similar illness
- H/o other autoimmune diseases in the patient

Condition on first visit:

- General condition
- Weight
- BP
- CVS
- RS
- Abdomen
- Others

Active skin lesion:

- Number, site
- Distribution – Groups / discrete along lines of trauma
- Healing lesions
- Mucosal lesions
-
- Palms / soles involvement
- Hair involvement

- Nail involvement
- Any other skin lesions

Investigations:

- Blood sugar
- LFT
- RFT
- Hemogram
- Blood VDRL
- Anti HCV antibody
- Biopsy
 - Site
 - Findings

DIF findings: